Applicant: Tsann-Long Su et al.

Serial No.: 10/799,576

Attorney's Docket No.: 08919-0118001

Academia Sinica Reference: 12A-921219

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Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application.

<u>Listing of Claims</u>:

1. (Currently amended) A compound having formula (I):

wherein,

each of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is, independently, hydrogen, halo, nitro, C_1 - C_6 alkyl, C_4 - C_6 -alkoxy, C_1 - C_6 hydroxyalkyl, CONHR^a, NR^bR^c , $CONH(CH_2)_mNR^bR^c$, L- $N(CH_2CH_2Cl)_2$, or a DNA minor groove binder;

L is $(CH_2)_p$ or $O(CH_2)_q$;

m is 1, 2, 3, or 4;

p is 0, 1, 2, 3, or 4;

q is 1, 2, 3, 4, 5, 6, 7, or 8;

in which, R^a is C_1 - C_6 alkyl; each of R^b and R^c is, independently, hydrogen, C_1 - C_6 alkyl, COR^d , or $COOR^d$; R^d is C_1 - C_6 alkyl, C_6 - C_{10} aryl, or C_7 - C_{12} aralkyl; and

the DNA minor groove binder is -CONH(CH₂)_r-J-W-(CH₂)_tR^e, wherein:

r is 1, 2, 3, 4, or 5;

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t is 1, 2, 3, 4, 5, or 6

J is -CONH- or -NHCO-;

or

W is a heteroaryl group having the following formula (II-A) or (II-B);

$$\begin{array}{c|c} X & H & \\ \hline & X & H \\ \hline & & & \\ \hline & & & \\ \hline & & & \\ & & & \\ \hline & & & \\ & & & \\ \end{array}$$
 (II-B)

s is 0, 1, 2, 3, or 4;

W' is NR^g, O, or S;

each of X and Y is, independently, N or CRf;

each of R^f and R^g is, indepently, hydrogen or C₁-C₆ alkyl;

Re is NRbRc, NHCHO, or NHC(=NH)NH2;

each of R^b and R^c is, independently, hydrogen, C₁-C₆ alkyl, COR^d, or

COOR^d, in which R^d is C₁-C₆ alkyl, C₆-C₁₀ aryl or C₇-C₁₂ aralkyl;

and provided that at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is L-N(CH₂CH₂Cl)₂, or a salt thereof.

- 2. (Original) The compound of claim 1, wherein L is $(CH_2)_p$.
- 3. (Original) The compound of claim 2, wherein p is 0 or 1.
- 4. (Original) The compound of claim 1, wherein L is $O(CH_2)_q$.
- 5. (Original) The compound of claim 4, wherein q is 2 or 4.

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6. (Original) The compound of claim 1, wherein one of R_1 , R_2 , R_3 , R_4 , or R_5 is L-N(CH₂CH₂Cl)₂.

- 7. (Original) The compound of claim 6, wherein R₂ or R₃ is L-N(CH₂CH₂Cl)₂.
- 8. (Original) The compound of claim 7, wherein R₂ is L-N(CH₂CH₂Cl)₂.
- 9. (Original) The compound of claim 8, wherein L is $(CH_2)_p$.
- 10. (Original) The compound of claim 9, wherein p is 0 or 1.
- 11. (Original) The compound of claim 8, wherein L is -O(CH₂)_a-.
- 12. (Original) The compound of claim 11, wherein q is 2 or 4.
- 13. (Currently amended) The compound of claim 8, wherein each of R_1 , R_3 , R_4 , and R_5 is, independently, hydrogen, C_1 - C_6 alkyl, C_4 - C_6 alkoxy, or C_1 - C_6 hydroxyalkyl.
 - 14. (Original) The compound of claim 13, wherein R₄ is C₁-C₆ hydroxyalkyl.
 - 15. (Original) The compound of claim 14, wherein R₄ is CH₂OH.
 - 16. (Original) The compound of claim 13, wherein each of R₁, R₃, R₄, and R₅ is hydrogen.
 - 17. (Original) The compound of claim 7, wherein R₃ is L-N(CH₂CH₂Cl)₂.
 - 18. (Original) The compound of claim 17, wherein L is $(CH_2)_n$.
 - 19. (Original) The compound of claim 18, wherein p is 0 or 1.

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- 20. (Original) The compound of claim 17, wherein L is -O(CH₂)_q-.
- 21. (Original) The compound of claim 20, wherein q is 2 or 4.
- 22. (Currently amended) The compound of claim 17, wherein each of R_1 , R_2 , R_4 , and R_5 is, independently, hydrogen, C_1 - C_6 alkyl, C_1 - C_6 -alkoxy, or C_1 - C_6 hydroxyalkyl.

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- 23. (Original) The compound of claim 21, wherein each of R_1 , R_2 , R_4 , and R_5 is hydrogen.
- 24. (Currently amended) The compound of claim 6, wherein each of R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, and R₁₃ is, independently, hydrogen, halo, nitro, C₁-C₆ alkyl, C₁-C₆ alkoxy, CONHR^a, CONH(CH₂)_mNR^bR^c, L-N(CH₂CH₂Cl)₂, or a DNA minor groove binder.
- 25. (Original) The compound of claim 24, wherein each of R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is, independently, hydrogen, C_1 - C_6 alkyl, $CONH(CH_2)_mNR^bR^c$, L- $N(CH_2CH_2Cl)_2$, or a DNA minor groove binder.
- 26. (Original) The compound of claim 25, wherein one of R_9 and R_{10} is $CONH(CH_2)_mNR^bR^c$, L-N(CH₂CH₂Cl)₂, or a DNA minor groove binder, and the other is C_1 - C_6 alkyl or hydrogen.
- 27. (Original) The compound of claim 26, wherein one of R_9 and R_{10} is $CONH(CH_2)_mNR^bR^c$ and the other is C_1 - C_6 alkyl or hydrogen.
- 28. (Original) The compound of claim 27, wherein one of R_9 and R_{10} is $CONH(CH_2)_2N(CH_3)_2$ and the other is CH_3 or hydrogen.

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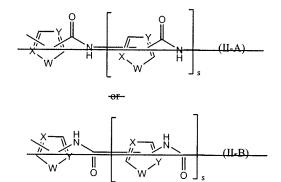
29. (Original) The compound of claim 26, wherein one of R_9 and R_{10} is L-N(CH₂CH₂Cl)₂ and the other is C₁-C₆ alkyl or hydrogen.

30. (Original) The compound of claim 29, wherein one of R_9 and R_{10} is $N(CH_2CH_2Cl)_2$ or $CH_2N(CH_2Cl)_2$ and the other is CH_3 or hydrogen.

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- 31. (Original) The compound of claim 29, wherein one of R_9 and R_{10} is $O(CH_2)_2N(CH_2CH_2Cl)_2$ or $O(CH_2)_4N(CH_2CH_2Cl)_2$ and the other is CH_3 or hydrogen.
- 32. (Original) The compound of claim 26, wherein one of R_9 and R_{10} is a DNA minor groove binder and the other is C_1 - C_6 alkyl or hydrogen.
- 33. (Currently amended) The compound of claim 32, wherein one of R_9 and R_{10} is CONH(CH₂)_r-J-W-(CH₂)_tR^e and the other is CH₃ or hydrogen; wherein r is 1, 2, 3, 4, or 5; t is 1, 2, 3, or 4, 5, or 6; J is -CONH- or -NHCO-; W is:



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in which s is 0, 1, 2, 3, or 4,; each of X and Y is, independently, N or CR^f and [[W]] \underline{W}' is NR^g , O, or S; R^e is NR^bR^c , NHCHO, or NHC(=NH)NH₂; each of R^b and R^c is, independently, hydrogen, C_1 - C_6 alkyl, COR^d , or $COOR^d$; and each of R^f and R^g is, independently, hydrogen or C_1 - C_6 alkyl.

- 34. (Currently amended) The compound of claim 33, wherein s is 0, each of X and Y is CH, and [[W]] W' is NCH₃.
 - 35. (Original) The compound of claim 34, wherein one of R_9 and R_{10} is:

36. (Original) The compound of claim 35, wherein r and t are both 3, and R^e is $N(CH_3)_2$, NHCHO, or NHC(=NH)NH₂.

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37. (Original) The compound of claim 34, wherein one of R₉ and R₁₀ is:

$$\begin{array}{c|c} H & H_2C \\ \hline \\ H_2C \\ \hline \\ C \\ H_2 \end{array} \\ \begin{array}{c} H \\ N \\ CH_3 \end{array}$$

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- 38. (Original) The compound of claim 36, wherein r and t are both 3, and R^e is $N(CH_3)_2$, NHCHO, or NHC(=NH)NH₂.
- 39. (Original) The compound of claim 24, wherein each of R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is hydrogen.
- 40. (Original) The compound of claim 1, wherein one of R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is L-N(CH₂CH₂Cl)₂.
 - 41. (Original) The compound of claim 40, wherein R₉ is L-N(CH₂CH₂Cl)₂.
 - 42. (Original) The compound of claim 41, wherein L is $(CH_2)_p$.
 - 43. (Original) The compound of claim 42, wherein p is 0 or 1.
 - 44. (Original) The compound of claim 41, wherein L is $-O(CH_2)_{a^-}$.
 - 45. (Original) The compound of claim 44, wherein q is 2 or 4.
- 46. (Currently amended) The compound of claim 41, wherein each of R_6 , R_7 , R_8 , R_{10} , R_{11} , R_{12} , and R_{13} is, independently, hydrogen, halo, nitro, or C_1 - C_6 alkyl, or C_4 - C_6 -alkoxy.

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47. (Currently amended) The compound of claim 40, wherein each of R₁, R₂, R₃, R₄, or R_5 is, independently, hydrogen, C_1 - C_6 alkyl, C_4 - C_6 -alkoxy, C_1 - C_6 hydroxyalkyl, or NR^bR^c .

- 48. (Previously presented) The compound of claim 47, wherein R₂ is NR^bR^c and R₄ is C₁-C₆ hydroxyalkyl.
 - 49. (Original) The compound of claim 48, wherein R₂ is NH₂ or NHCOOCH₂CH₃.
 - 50. (Original) The compound of claim 48, wherein R₄ is CH₂OH.

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is:

51. (Previously presented) The compound of claim 1, wherein the compound

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52. (Currently amended) A pharmaceutical composition comprising a compound of formula (I) and a pharmaceutically acceptable carrier:

$$R_4$$
 R_5
 R_1
 R_1
 R_1
 R_1
 R_1
 R_1
 R_1
 R_2
 R_1
 R_1
 R_2
 R_1
 R_2
 R_1
 R_2
 R_1
 R_2
 R_1
 R_2
 R_1
 R_2
 R_3
 R_4
 R_5
 R_1
 R_1
 R_2
 R_3
 R_4
 R_5
 R_7
 R_8
 R_9

wherein,

each of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is, independently, hydrogen, halo, nitro, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 hydroxyalkyl, CONHR^a, NR^bR^c, CONH(CH₂)_mNR^bR^c, L-N(CH₂CH₂Cl)₂, or a DNA minor groove binder;

L is $(CH_2)_p$ or $O(CH_2)_q$;

m is 1, 2, 3, or 4;

p is 0, 1, 2, 3, or 4;

q is 1, 2, 3, 4, 5, 6, 7, or 8;

in which, R^a is C_1 - C_6 alkyl; each of R^b and R^c is, independently, hydrogen, C_1 - C_6 alkyl, COR^d , or $COOR^d$; R^d is C_1 - C_6 alkyl, C_6 - C_{10} aryl, or C_7 - C_{12} aralkyl; and

the DNA minor groove binder is -CONH(CH₂)_r-J-W-(CH₂)_tR^e, wherein:

<u>r is 1, 2, 3, 4, or 5;</u>

t is 1, 2, 3, 4, 5, or 6

J is -CONH- or -NHCO-;

W is a heteroaryl group having the following formula (II-A) or (II-B);

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$$\begin{array}{c|c} X & H & H \\ \hline & X & H \\ \hline & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

s is 0, 1, 2, 3, or 4;

W' is NR^g, O, or S;

each of X and Y is, independently, N or CRf;

each of R^f and R^g is, indepently, hydrogen or C₁-C₆ alkyl;

Re is NRbRc, NHCHO, or NHC(=NH)NH2; and

each of R^b and R^c is, independently, hydrogen, C₁-C₆ alkyl, COR^d, or

\underline{COOR}^d , in which \underline{R}^d is $\underline{C_1}$ - $\underline{C_6}$ alkyl, $\underline{C_6}$ - $\underline{C_{10}}$ aryl or $\underline{C_7}$ - $\underline{C_{12}}$ aralkyl; and

provided that at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is $L-N(CH_2CH_2Cl)_2$; or a pharmaceutically acceptable salt thereof.

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53. (Currently amended) A method of treating cancer, the method comprising administering to a subject in need thereof an effective amount of a compound of formula (I):

wherein,

each of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is, independently, hydrogen, halo, nitro, C_1 - C_6 alkyl, C_1 - C_6 -alkoxy, C_1 - C_6 hydroxyalkyl, CONHR^a, NR^bR^c, CONH(CH₂)_mNR^bR^c, L-N(CH₂CH₂Cl)₂, or a DNA minor groove binder;

L is $(CH_2)_p$ or $O(CH_2)_q$;

m is 1, 2, 3, or 4;

p is 0, 1, 2, 3, or 4;

q is 1, 2, 3, 4, 5, 6, 7, or 8;

in which, R^a is C_1 - C_6 alkyl; each of R^b and R^c is, independently, hydrogen, C_1 - C_6 alkyl, COR^d , or $COOR^d$; R^d is C_1 - C_6 alkyl, C_6 - C_{10} aryl, or C_7 - C_{12} aralkyl; and

the DNA minor groove binder is -CONH(CH₂)_r-J-W-(CH₂)_tR^e, wherein:

<u>r is 1, 2, 3, 4, or 5;</u>

t is 1, 2, 3, 4, 5, or 6

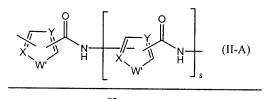
J is -CONH- or -NHCO-;

W is a heteroaryl group having the following formula (II-A) or (II-B);

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$$\begin{array}{c|c} X & H & H \\ \hline X & Y & O \\ \hline \end{array}$$

$$\begin{array}{c|c} X & H \\ \hline \end{array}$$

s is 0, 1, 2, 3, or 4;

W' is NR^g, O, or S;

each of X and Y is, independently, N or CRf;

each of R^f and R^g is, indepently, hydrogen or C₁-C₆ alkyl;

R^e is NR^bR^c, NHCHO, or NHC(=NH)NH₂;

each of R^b and R^c is, independently, hydrogen, C₁-C₆ alkyl, COR^d, or

COOR^d, in which R^d is C₁-C₆ alkyl, C₆-C₁₀ aryl or C₇-C₁₂ aralkyl;

and provided that at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , and R_{13} is L-N(CH₂CH₂Cl)₂; or a pharmaceutically acceptable salt thereof.